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**Chronic Swallowing Ability in Nasopharyngeal Cancer Survivors  
after Radiotherapy with or without Chemotherapy**

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Abstract

In light of the lack of multidimensional data of long-term swallowing functions in nasopharyngeal cancer (NPC) survivors, the current study investigated NPC survivors' long-term swallowing dysfunctions after radiotherapy or chemoradiation by a multidimensional protocol and explored their relationships with demographic and treatment-related variables. Twenty-seven participants were recruited and assessed through oromotor assessment, fiberoptic endoscopic evaluation of swallowing and quality-of-life questionnaires. Nearly half of the participants had oromotor deficits (47.6%) and penetration in at least one of the swallowing trials (45.8%). All participants had pharyngeal residue in valleculae and most participants have residue in pyriform sinuses (81.8%) in at least one of the swallowing trials. Limitations in the activity and participation domains were prevalent though large variation in functioning was noted. Comparison between groups indicated that participants treated with concurrent chemotherapy have significantly less degree of penetration or aspiration and less residue in valleculae on oral trials for extra thick liquid than those treated with radiotherapy alone. Correlation analysis indicated that degree of penetration in thin liquid, mildly thick liquid and amount of residue residing on valleculae in extra thick liquid increase with the number of years since completion of radiotherapy. Functioning in the activity and participation domains also decreased with time since completion of radiotherapy. Regression analysis indicated that number of years since completion of radiotherapy was a significant predictor for pharyngeal residue. The deteriorating trend identified provided evidence to the need of continuous monitoring in swallowing functions in nasopharyngeal cancer survivors. Further research to identify risk factors for long-term swallowing problems and ways to minimize long-term swallowing problems are needed for early identification and maximising swallowing functions for nasopharyngeal cancer survivors.

**Keywords:** Chronic swallowing functions, nasopharyngeal cancer, radiotherapy, chemotherapy

Nasopharyngeal cancer (NPC) is particularly common in the Chinese population when compared with other parts of the world (Yu & Yuan, 2002). According to the latest statistics in Hong Kong Cancer Registry, NPC is the 7<sup>th</sup> most common cancer and ranked 7<sup>th</sup> in mortality rate among cancer types in 2011. There are 632 male and 230 female new cases in the year of 2011. Incidence rate for NPC is 12.2 per 100,000 in the population. Currently, radiotherapy with or without chemotherapy is the main treatment method for NPC. The overall survival rate after radiotherapy or chemoradiation was found to be 75% in a 5 year post-treatment period (Lee et al., 2005). Previous study has found that about 75% NPC survivors experienced dysphagia after radiotherapy (Hughes et al., 2000). Despite the prevalence of dysphagia reported for nasopharyngeal cancer survivors, there is a paucity of data on the chronic swallowing outcome as assessed by multidimensional outcome measures which is specific for nasopharyngeal cancer survivors.

Dysphagia symptoms previously identified for head and neck cancer survivors included reduced airway protection, delayed swallow initiation uncoordinated swallowing, reduced swallowing efficiency and silent aspiration (Eisbruch et al., 2002; Lazarus et al., 1996; Nguyen et al., 2004). Impact of head and neck cancer treatment on swallowing-related quality-of-life was also reported in Nguyen et al. (2005). Some pathophysiological explanations have been given to the swallowing outcomes in the population. For one, radiotherapy-induced insufficient saliva production, or xerostomia, contributes to the swallowing difficulties by impairing the lubrication of food bolus, which is important for food transition. In addition, radiotherapy may induce fibrosis or neuromuscular incoordination to the pharyngeal constrictors and other swallowing-related structures. This impairs the pharyngeal functions and hence reduces laryngeal clearance and laryngeal closure (Hughes et al, 1999), leading to aspiration which can be fatal.

Previous studies have also identified a number of risk factors associated with dysphagia in head-and-neck cancer survivors, including older age, advanced T-stage, bilateral neck irradiation, weight loss prior to radiation and higher doses to dysphagia/ aspiration related structures (DARS) (Eisbruch et al., 2004; Langendijk et al., 2009; Machtay et al., 2008). However, there is still mixed results regarding the risk factors correlating with swallowing functions. While a higher doses to DARS has been found to correlate with more severe dysphagia symptoms in some studies (Eisbruch et al., 2007; Feng et al., 2007), such correlation cannot be found in Bhide et al. (2009). Batth, Caudell, and Chen (2014) suggested in their review paper that such variability can be accounted for by the different outcome measures used in the studies. While some studies used patient-reported questionnaires as the sole outcome measure, some used observer-rated measures or instrumental methods such as videofluoroscopy. Hence, to better assess the swallowing outcomes after radiotherapy, multidimensional data should be collected. In summary, despite the wealth of research looking into the swallowing outcome in head and neck cancer survivors and nasopharyngeal cancer survivors, there is a paucity of study which evaluates survivor's multidimensional swallowing outcomes in one study. In light of this, the current study aims to investigate long-term swallowing functions in NPC survivors using a multidimensional assessment protocol based on the International Classification of Functioning, Disability and Health (ICF) framework. The International Classification of Functioning, Disability and Health framework provides a multidimensional framework in which the swallowing problem can be described. In the framework, dysphagia can be described by the two domains: (i) body functions and structures and (ii) activity and participation.

Also, subjects in previous studies mostly included a heterogeneous group of head-and-neck cancer survivors, including a small number of NPC survivors. However, some other studies

have demonstrated that the primary tumor localization was correlated with swallowing outcomes (Caglar et al., 2008; Dirix et al., 2009). Hence, study on the effect of radiotherapy on swallowing functions should be conducted specifically for each cancer type instead of head and neck cancer in general. Hence, the current study aims to identify the swallowing problems in nasopharyngeal cancer survivors specifically.

In addition, although information on the swallowing functions after radiotherapy was plenty, most studies did not look into the long-term swallowing function in nasopharyngeal cancer survivors. Previous study has investigated that short-term swallowing outcomes by evaluating head and neck cancer survivors 4-8 weeks after radiotherapy (Caglar et al., 2008). Other studies looking into swallowing outcomes in head and neck cancer survivors have evaluated swallowing functions within 24 month after therapy (e.g. Dornfeld et al., 2007; Schwartz et al., 2010). Although Dirix, Abbeel, Vanstraelen, Hermans, and Nuyts (2009) have investigated swallowing functions of 53 head and neck cancer survivors for up to 44.9 month after radiotherapy, they studied survivors with different cancer types and hence NPC-specific data was lacking. Information on the long-term dysphagia symptoms is important from a clinical perspective as it provides invaluable information for the long-term management of dysphagia in nasopharyngeal cancer survivors. In view of this, the current study also aims to look into long-term swallowing functions in NPC survivors.

Hence, in light of the lack of data of long-term, NPC specific and multidimensional swallowing functions after radiotherapy, the first objective of the study was to identify long-term swallowing functions in nasopharyngeal cancer survivors using a multidimensional assessment protocol. To better understand if the swallowing outcomes were associated with the demographic

or treatment-related factors, the second objective was to identify factors which might be related to the long-term swallowing outcomes.

## Method

### Participants

Twenty-seven nasopharyngeal cancer (NPC) survivors treated successfully with radiotherapy with or without chemotherapy were recruited in the study. Eleven males and 16 females with a mean age of 57.6, ranged from 47 to 68 ( $SD = 6.74$ ) were recruited. Only participants who have finished radiotherapy and/ or chemotherapy treatment for at least one year were recruited to avoid acute symptoms and to assess their long-term swallowing functions. To better assess treatment-related swallowing difficulties, survivors who have pre-treatment swallowing difficulty or other concomitant neurological or cognitive problems were excluded from the study. Table 1 shows the treatment-related factors for the participants.

**Table 1.**

*Treatment-related factors of the participants.*

Treatment-related factors	NPC survivors (n=27)
Range of time since completion of radiotherapy (in years), mean ( $SD$ )	2-28, 10.91 (6.65)
Concurrent chemotherapy	
with concurrent chemotherapy	10
without concurrent chemotherapy	17
Concurrent surgical intervention	
with concurrent surgical intervention	5
without concurrent surgical intervention	22

### Procedures

Demographic data and treatment related factors were collected. The participant's swallowing abilities were then evaluated with the following procedures: (a) oromotor assessment, (b) participant-rated quality-of-life questionnaire and (c) fiberoptic endoscopic

evaluation of swallowing (FEES) and (d) a clinician-rated functional scale. Patients were evaluated with different order in the procedures.

**Oromotor assessment.** The client's oromotor abilities were assessed by a speech therapist. Strength, range of movement and coordination of jaw, lips and tongue were rated on a 6-point scale. A score of 0 represents severely impaired function and 5 represented non-impaired function. A composite score for each oromotor structure was obtained by averaging the scores in strength, range of movement and coordination. This outcome corresponds to the body functions and structures level in the ICF framework.

**Fiberoptic Endoscopic Evaluation of Swallowing (FEES).** The participant's swallowing ability was assessed using FEES. FEES provides a clear view of the hypopharynx and larynx during swallow which are valuable in evaluating the pharyngeal phase of swallow (Langmore, Schatz, & Olsen, 1988). Aspiration or penetration, or other related parameters such as amount of residue after swallow can be observed using FEES. During the assessment, each participant sat upright on a chair. Using the Wolf's Medical High Definition Endocam (Richard Wolf 5509, Knittlingen), a trained speech therapist inserted a flexible laryngoscope through the nasal cavity to the pharyngeal area until the laryngeal area was visualized. Each participant was fed at least one teaspoon (5ml) on each of the three consistencies: thin liquid, mildly thick liquid (100ml liquid with three standard spoonful of the thickener RESOURCE® THICKENUP® and extra thick liquid (100ml liquid with five standard spoonful of the thickener RESOURCE® THICKENUP®). The three different consistencies were coloured differently with food dye to ensure there were clear distinctions between the trials. Degree of penetration or aspiration was rated using the Penetration-Aspiration Scale (Rosenbek, Robbins, Roecker, Coyle, & Wood, 1996). The approximate amount of bolus (in %) that remained on the valleculae or in the



pyriform sinuses were measured. Both the P-A scale and residue estimate corresponds to swallowing outcomes in the body functions and structures level in the ICF framework.

***The Penetration-Aspiration Scale (P-A scale).*** All swallowing trials were rated on the P-A scale by two speech therapists. The P-A scale is an eight-point equal appearing scales for evaluation the degrees of penetration and aspiration, with higher rating corresponding to a more severe penetration/ aspiration status. The scale evaluates not only the depth of penetration or aspiration during swallow but also participant's ability to remove the penetrated/ aspirated materials (Rosenbek et al., 1996). Both raters rated the P-A scale on the video of the endoscopic examination after the video have been encoded with participants numbers so they were blind to their other information during the ratings.

***Percentage of bolus residing in valleculae or pyriform sinuses.*** On each swallowing trial, the approximate percentage of bolus residing in the valleculae or the pyriform sinuses were measured by the speech therapist. This factor was measured because disorders in the pharyngeal phase which can lead to residue in valleculae and pyriform sinuses have been reported in head and neck cancer survivors after treatment (Murphy & Gilbert, 2009). Also, pharyngeal residue has been reported as a predictor for aspiration for head and neck cancer survivors (Eisenhuber et al., 2002).

**Clinician-rated measure.** The Functional Oral Intake Scale was used as the clinician-rated scale for each client. The FOIS is a valid and reliable measure of the functional aspect of the participant's current diet (Crary, Mann, & Groher, 2005). It is a clinician-rated seven-point scale with one corresponding to nothing by mouth and seven corresponding to total oral diet with no restrictions. The speech therapist rated each participant using the scale based on the participant's current diet. This measure corresponds to the activity level in the ICF framework.

**Self-reported quality of life questionnaire.** All participants were asked to complete the M.D. Anderson Dysphagia Inventory (Chen et al., 2001). The questionnaire was used to assess the swallowing-related functioning and disability of the participants. The M.D. Anderson Dysphagia Inventory (MDADI) is a reliable and validated dysphagia-specific quality-of-life (QOL) questionnaire which contains 20 questions separated into four subscales including global, physical, functional and emotional subscale. The global subscale measures the overall QOL affected by dysphagia. Physical subscale measures survivor's self-perception of swallowing difficulty relating to performing swallowing related tasks. Functional subscale measures the impact on daily activities brought by dysphagia. Emotional subscale measures the emotional response of the survivor towards his/her dysphagia. Each question is rated on a five-point scale. The score obtained in each scale will be summed up and translated to a score ranging from 0 to 100, with a score of 100 indicating high functioning and a score of 0 representing extremely low functioning.

The four scales were categorized to different domains in the ICF framework for describing the swallowing functions in the two domains. The MDADI emotional subscale measured emotional response of the participants and hence it represented functions in the subcomponent 'Specific Mental functions' under the body functions and structures domains in the framework. The MDADI global, physical and functional scale measured the participants' ability to perform swallowing-related task and participate in life-events and hence they represented functions under the activity and participation domains.

### **Data Analysis**

Gender, age, number of years after radiotherapy and involvement of chemotherapy during radiotherapy treatment were the independent variables in the study. Swallowing-related

outcome measures included: (i) oromotor ability, (ii) the Penetration-Aspiration scale, (iii) Percentage of bolus residing on valleculae and pyriform sinuses (iv) Functional Oral Intake Scales and (v) MDADI scores. For comparison of swallowing outcomes between categorical groups (i.e. gender and involvement of chemotherapy) on the swallowing outcomes, Mann-Whitney U test was used. Correlation between the time since completion of treatment and the swallowing outcomes were conducted using the Spearman rho rank order correlation. Non-parametric tests were used due to the small sample size in the current study. The significance level was set at 0.05. Intraclass correlation (ICC) was used to measure the interrater reliability in rating the P-A scale. Both raters were asked to re-rate 20% of the data and the intra-rater reliability was also measured using the intraclass correlation.

## Results

### Reliability in P-A ratings

Based on the suggested interpretation of intraclass correlation in Landis and Koch (1977), ratings for P-A scale showed good reliability [ ICC (2, 1) = .696,  $p < .001$ ] in thin liquid and good-to-perfect reliability [ ICC (2,1) = .856,  $p < .001$ ] in mildly thick liquid and good reliability [ ICC (2,1) = .775,  $p < .05$  ] in extra thick liquid. Intra-rater reliability for the ratings on different consistencies of fluid is shown in Table 2. The intra-rater reliability ranged from good to extremely good (.762-1.00).

**Table 2.**

*Intra-rater reliability as measured in ICC coefficient for rating P-A scale on different fluid trials*

Swallowing Trials	Rater A	Rater B
Thin Liquid	.762	.762
Mildly Thick Liquid	1.00	.980
Extra Thick Liquid	.980	.960

**Long-term swallowing functions after radiotherapy**

The results indicated that the participants' dysphagia manifested in different domains in the ICF model. The swallowing functions of NPC survivors in the two domains will be described accordingly as follows.

**Body functions and structures domain.** Outcome measures of oromotor ability, the Penetration-Aspiration Scale, percentage bolus residing on valleculae and pyriform sinuses after swallowing and the MDADI emotional scores corresponded to the body functions and structures level of measurement.

For oromotor ability, one participant was noted to have jaw impairment (4.5 %) and eight participants (30.8%) had lips impairment. Twelve participants (50%) had impairment in tongue. Overall, 10 participants (47.6%) has impairment in at least one of the oromotor structures.

Based on the P-A scale, 18 participants showed no sign of penetration on thin liquid (72%), six participants (24%) penetrated on thin liquid and one participant aspirated on thin liquid (4%). On mildly thick liquid, 17 participants (73.9%) showed no signs of penetration, and five participants (25.1%) had penetration. No participant had aspiration on mildly thick liquid. On extra thick liquid, sixteen participants (84.2%) showed no sign of penetration, whereas three participants (15.8%) had penetration. No participant aspirated on extra thick liquid. Taking all trials into consideration, 11 participants (45.8%) had penetration in at least one of the swallowing trials. Not all swallowing trials could be rated as some views were blocked during the swallowing trials.

The percentage of bolus residing on valleculae and pyriform sinuses was evaluated. All participants have pharyngeal residue in valleculae in at least one swallowing trial. Eighteen of the participants (81.8%) who have been rated in this parameter have pharyngeal residue in

pyriform sinuses at least one of the trials. Table 3 shows the range, mean and standard deviation of the results in this outcome.

**Table 3.**

*Percentage of bolus residing on valleculae and pyriform sinuses<sup>^</sup>*

Oral Trials		Range	M (SD)
Thin liquid	Percentage of bolus residing on valleculae (%)	0-100	23.0(27.3)
	Percentage of bolus residing on pyriform sinuses (%)	0-75	23.3(28.1)
Mildly thick liquid	Percentage of bolus residing on valleculae (%)	0-60	23.9(19.9)
	Percentage of bolus residing on pyriform sinuses (%)	0-95	21.4(27.5)
Extra Thick Liquid	Percentage of bolus residing on valleculae (%)	5-100	54.7(31.1)
	Percentage of bolus residing on pyriform sinuses (%)	0-50	10.7(16.3)

<sup>^</sup> not all participants has been rated in all swallowing trials as the view was blocked for some trials

As for MDADI emotional scale, the scores ranged from 20 to 80, with a mean score and standard deviation of 56.2 and 17.1 respectively. The highest score possible was 100 which represents high functioning, and the lowest score possible was 0 which represents extremely low functioning (Chen et al., 2001). The mean score hence represented a moderate functioning in the scale.

**Activity and participation domain** Outcome measures of Functional Oral Intake Scale and the MDADI physical scale corresponded to the activity level of measurement. The distribution of FOIS rating of the participants is shown in Table 4. Five participants were having non-oral diet (18.5%). The majority of the participants (44.4%) were having oral diet with

specific food limitations. The mean and standard deviation for FOIS score was 5.19 and 1.91 respectively. The scores for the MDADI physical scale ranged from 23 to 75, with a mean score of 53.6 (  $SD = 15.7$ ). The mean score represented a moderate functioning in the scale.

**Table 4.**

*Number of participants in each level on the FOIS (scale adapted from Crary et al., 2005)*

Level	Description	Number of participants
1	Nothing by mouth.	3
2	Tube dependent with minimal attempts of food or liquid	1
3	Tube dependent with consistent oral intake of food or liquid	1
4	Total oral diet of a single consistency	0
5	Total oral diet with multiple consistencies, but requiring special preparation or compensations	4
6	Total oral diet with multiple consistencies without special preparation, but with specific food limitations	12
7	Total oral diet with no restrictions.	6

Outcome measures in MDADI global and functional scale corresponds to the participation level measurement. The MDADI global score ranged from 20 to 80 with mean score and standard deviation of 42.2 and 20.3 respectively. For the MDADI functional scale, the score ranged from 36 to 80 with a mean score of 56.4 ( $SD = 14.6$ ). The mean scores for both global and functional scale also represented a moderate function.

### **Factors Affecting Swallowing Outcomes**

Table 5 shows the mean score and standard deviation in the outcome measures for different groups. For comparison of score across ages, three age groups were arbitrarily set for showing the mean score in the outcome measures across age.

**Relationships between independent variables and swallowing outcomes.** Participants who had chemotherapy had significantly lower degree of penetration as shown from the P-A score for mildly thick liquid [ $U = 36.0$ ,  $p < .05$ ,  $r = .46$ ], and less residue for extra thick liquid

[ $U = 15.0, p < .05, r = .50$ ]. Participants with concurrent chemotherapy did not differ significantly in number of years since radiotherapy [ $U = 57.0, ns, r = .27$ ] and age [ $U = 50.5, ns, r = .34$ ] from participants without concurrent chemotherapy.

Number of years since completion of radiotherapy was positively correlated with degree of penetration for thin liquid [ $r_s(25) = .633, p < .01$ ], mildly thick liquid [ $r_s(23) = .415, p < .05$ ] and residue at valleculae for extra thick liquid [ $r_s(18) = .548, p < .05$ ]. Also, the number of years since completion of radiotherapy was negatively correlated with the MDADI global scale score [ $r_s(27) = -.382, p < .05$ ] and MDADI physical scale score [ $r_s(27) = -.417, p < .05$ ].

Regression analysis indicated that the number of years since completion of radiotherapy significantly predicted the percentage of bolus residing on valleculae in extra thick liquid trials,  $\beta = .574, t(16) = 2.80, p < .05$ , with higher number of years since completion predicting more valleculae residue for extra thick liquid. It explained a significant proportion of variance in the outcome,  $R^2 = .329, F(1, 16) = 7.86, p < .05$ .

**Relationships among dependent variables.** Correlation between the outcome measures was also assessed. P-A scale in thin liquid was found to be positively correlated with the percentage of bolus residing on pyriform sinuses in oral trials on thin liquid [ $r_s(20) = .503, p < .05$ ].

**Table 5.***Outcome measures in different groupings*

Groups		OMComp <sup>^</sup>	Body functions and structures domains parameters			
			MDADI E <sup>+</sup>	PAtin <sup>+</sup>	PAmild <sup>+</sup>	PAextra <sup>+</sup>
		<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>
Gender	Male	3.74 (1.02)	55.8 (13.1)	2.36 (2.24)	2.36 (2.25)	1.50 (1.23)
	Female	4.30 (.79)	56.5 (19.8)	1.50 (1.09)	1.50 (1.09)	1.31 (.855)
Age Group	Below 50	*	54.4 (25.0)	2.00 (1.73)	2.00 (1.73)	1.33 (.577)
	51-60	3.87 (.950)	56.7 (15.1)	1.40 (.910)	1.31 (.855)	1.30 (.949)
	61-70	4.51 (.673)	55.9 (19.8)	2.86 (2.67)	2.00 (1.53)	1.50 (1.24)
CT	with CT	4.13 (.956)	61.0 (13.2)	1.60 (1.075)	1.00 (.000)	1.00 (.000)
	without CT	4.05 (.914)	53.3 (18.8)	2.07 (2.05)	1.93 (1.39)	1.58 (1.17)

<sup>^</sup> for simplicity, a composite score (OMComp) for the oromotor ability in lips, jaw and tongue was obtained by averaging the scores in the three oromotor structures.

\* missing value as participants could not complete the full assessment

<sup>+</sup>MDADIE: Emotional scale of MDADI; PAtin: P-A scale for thin liquid trials; PAmild: P-A scale for mildly thick liquid trials; PAextra: P-A scale for extra thick liquid trials.



**Table 5.***(continued) Outcome measures in different groupings*

Groups		Body functions and structures Level Parameters (Continued)		Activity Level Parameters		Participation Level Parameters	
		%Resid(V) <sup>+</sup>	%Resid(P) <sup>+</sup>	FOIS	MDADIP <sup>+</sup>	MDADIG <sup>+</sup>	MDADI F <sup>+</sup>
		<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>
Gender	Male	31.4 (15.5)	24.6 (31.8)	4.70 (2.00)	55.0 (13.6)	38.2 (18.9)	52.4 (13.9)
	Female	30.9 (18.7)	8.33 (10.9)	5.80 (1.47)	52.7 (17.4)	45.0 (21.3)	59.3 (14.8)
Age	Below 50	22.2 (5.09)	11.7 (16.5)	6.00 (1.00)	51.7 (23.6)	46.7 (30.6)	53.3 (18.0)
Group	51-60	32.3 (18.62)	11.1 (12.0)	5.15 (1.91)	52.0 (13.6)	38.7 (16.0)	56.0 (12.5)
	61-70	34.0 (19.2)	29.7 (39.8)	5.44 (1.81)	56.9 (17.8)	46.7 (24.5)	58.2 (18.1)
CT	with CT	24.0 (14.3)	10.8 (13.2)	5.33 (2.00)	57.3 (11.6)	48.0 (19.3)	59.6 (14.0)
	without CT	35.6 (17.7)	21.7 (30.7)	5.38 (1.67)	51.5 (17.7)	38.8 (20.6)	54.6 (15.0)

<sup>+</sup> %Resid(V): percentage of bolus residing on valleculae; %Resid(P): percentage of bolus residing on pyriform sinuses; MDADIP: Physical scale of MDADI; MDADIG: Global scale of MDADI; MDADIF: Functional scale of MDADI

## **Discussion**

The first objective of the study was to identify long-term swallowing functions in nasopharyngeal survivors after radiotherapy or chemo-radiation. The following discusses the swallowing functions and ability in the two domains in ICF. Following discussion of the long-term swallowing problems and the possible pathophysiology, factors which are correlated with swallowing outcome and their implication will be discussed.

### **Long-term swallowing functions in nasopharyngeal cancer survivors.**

**Body functions and structures domain.** Oromotor deficits, penetration or aspiration and pharyngeal retention were common in participants in the current study, occurring in 47.6%, 45.8% and all participants respectively. Impairment in tongue function was the most common oromotor deficit, which occur in half of the participants. Previous study has reported tongue atrophy in 54.8% of head and neck cancer survivors (see review by Manikantan et al., 2009). They suggested that the sequelae of radiation mainly arouse from the tissue change in the head and neck region upon radiation, which is directly related to the dosimetry of the radiation. Other study also suggested that radiotherapy can lead to fibrosis in the head and neck region (Cooper, Fu, Marks, & Silverman, 1995), and hence this may be a possible explanation to the oromotor deficits in the current study. Another possible pathophysiology might be cranial nerve palsy. Since swallowing-related structures are controlled by cranial nerves, damage on the cranial nerves induced by radiation might lead to oromotor deficits. For nasopharyngeal cancer survivors, cranial nerve palsy which can lead to oromotor dysfunctions has been reported for all three participants in Mok, Seshadri, Siow, and Lim (2001)'s study. In light of these, there were different hypotheses to explain the observed impairment in the current study, hence the pathophysiology remains to be an area which requires further investigation.

The incidence for penetration or aspiration was common as reflected in the P-A scale. Pharyngeal retention was also prevalent dysphagic symptoms among the participants. Positive correlation between percentages of bolus residing on pyriform sinuses on thin liquid and P-A score indicated that the residue might be a risk factor for penetration or aspiration. Pharyngeal retention has also been reported in nasopharyngeal cancer survivors in previous study (Wu, Hsiao, Ko, & Hsu, 2000) in which a correlation between pharyngeal retention and post-swallow aspiration was also found. Examination of the percentage of bolus residing shows that a large proportion ( $M = 54.7\%$ ) of the bolus was retained in the valleculae after swallow for extra thick liquid, indicating a specific difficulty in swallowing thicker fluid. Possible pathophysiology to the pyriform sinus residue might be an impaired pharyngeal bolus transition and inadequate upper esophageal sphincter (UES) relaxation (Dodds, Logemann, & Stewart, 1990; Manikantan et al., 2009). For head and neck cancer survivors, this impairment in pharyngeal constrictor muscles have been reported in Eisbruch et al. (2004). Since the pharyngeal constrictors were adjacent to the tumor localization for head and neck cancer, the pharyngeal constrictors might be exposed to a high dose of radiation during radiotherapy. Previous study has demonstrated that radiation dose to the pharyngeal constrictors is positively correlated with impairment in swallowing in head and neck cancer survivors (Eisbruch et al., 2007; Feng et al., 2007). Hence, the observed impairment in the pharyngeal phase of swallow might also be associated with dosage during radiotherapy.

On an emotional aspect, the client showed moderate function as reflected in the MDADI emotional score. However, large variation in the score was noted which indicated that the manifestation of swallowing outcome in the emotional aspect varied across survivors.

**Activity and participation domain.** The FOIS and scores on MDADI physical scale are outcome measures corresponding to the activity domains. The results indicated that diet alternation was common. From the FOIS rating, five participants (18.5%) in our study were tube-dependent survivors whereas others were having oral diet with or without restrictions. However, the majority of the participants (44.4%) are having oral diet with specific food limitations. This indicated that there was a wide range of functional outcome in terms of their current diet. For the MDADI physical scale, the participants on average have a moderate function in the scales. This suggested the participant's swallowing problem also manifest in limiting their day-to-day activity. However, it was also noted that variation in the MDADI score was large, indicating the participants' swallowing problem have limited their swallowing-related activity differently.

Scores in the MDADI global and functional scales corresponds to the participation domains. Overall, the participants also achieved a moderate functioning in the MDADI global and functional scales. Again, variation in the score was large, indicating that the swallowing problem have affected their participation in life-events or social activities.

### **Factors correlating with the swallowing outcomes**

Although long-term swallowing disabilities were identified, many variations were noted in different outcome parameters across patients. The second objective of this study aims to identify factors which may be associated with the swallowing outcomes. The following described the associated factors and the possible hypothesis behind the association.

**Number of years since completion of radiotherapy.** The number of years since completion of radiotherapy was significantly correlated with swallowing outcomes in different domains. In general, as the number of years since completion of cancer treatment increases, the

swallowing functions decreased in both the body functions and structures, and activity and participation domains.

From a clinical perspective, the trend of general deteriorating functions in swallowing provided evidence to support continuous monitoring of swallowing functions in nasopharyngeal cancer survivors. This idea is also supported in a review paper by Rosenthal, Lewin, and Eisbruch (2006), in which assessments before, during and after the radiotherapy were recommended such that swallowing maneuvers and other therapeutic strategies can be suggested as soon as swallowing problem emerge. In light of the research evidence that postural change and swallowing maneuvers were effective in lowering aspiration risks (Logemann, Pauloski, Rademaker, & Colangelo, 1997; Rasley et al., 1993), this continuous management and introduction of suitable therapeutic strategies at an early stage is very important for better prognosis in terms of their swallowing functions.

From a research perspective, the deteriorating swallowing function is a proponent to urge for further research to identify reasons behind the deterioration and ways to prevent or minimize the deterioration. The utmost research questions would be the pathophysiology behind the deterioration in functions with time and whether it can be prevented or minimized, and then the way through which can be done. Some studies have already provided possible explanation to the pathophysiology of the deterioration. Previous paper by Murphy and Gilbert (2009) suggested that the chronic deprivation of oxygen, and imbalance in the production and detoxification of free radicals which lead to tissue damage can happen after a long time of radiotherapy treatment. These processes may cause long term deterioration in swallowing-related structures and hence the longer the radiotherapy has been completed, the worse the swallowing outcome would be. Empirical evidence of structural change in swallowing structure with time after radiotherapy has

been documented in a prospective study by Eisbruch et al. (2004), who have also shown that such change was likely related to the swallowing functions. Hence, the next research question would be to identify the factors which can affect the processes and whether they can be altered to minimize long-term swallowing deterioration.

**Concurrent chemotherapy.** From the analysis, participants treated with chemotherapy had significantly lower degree of penetration in oral trials on mildly thick liquid and less residue on valleculae for extra thick liquid than participants without chemotherapy. Comparison between the two groups indicated that the two groups did not differ significantly in age or number of years since completion of radiotherapy, suggesting that the involvement of chemotherapy concurrent with the radiotherapy might be the main factor associated with the swallowing outcomes. Similar to the current findings, the predictive value of concurrent chemotherapy has been reported in head and neck cancer survivors (De Ruyck et al., 2013). However, the current study found an opposite trend to the study conducted by Caudell et al. (2009). Since the study population in Caudell et al. (2009) was head and neck cancer survivors, the difference in the direction of relationship raised the questions on whether concurrent chemotherapy have different association with different types of head and neck cancer survivors. Although the current study has provided further evidence that concurrent chemotherapy is associated with the chronic swallowing outcome, further investigation is needed to how chemotherapy may be related to swallowing outcomes and whether they have different associations for different cancer types.

### **Limitations and further study**

One limitation on the current study is the lack of treatment details for each participant. As explained, emerging evidence is suggesting that dose to swallowing-related structures are

correlated with swallowing outcomes in head and neck cancer survivors. It is possible that such factor is also associated with swallowing outcome in nasopharyngeal cancer survivors. Hence, investigation into the effect of demographic variables should be done alongside with detailed treatment variables. Treatment details such as the treatment modality, treatment technique, dosage, and duration of the therapy can be further investigated to identify if any specific parameters may be associated with swallowing outcomes.

Another limitation of the current study is that prospective evaluation of swallowing functions was not conducted. This limitation may affect the interpretation of the observed deteriorating swallowing functions with time. It is difficult to isolate whether the observed trend was attributable solely to the time change due to within subject function deterioration or between subject factors. One prominent between subject factors which may be associated with the time-changing swallowing function is the difference in treatment strategy in radiotherapy. Different radiotherapy planning techniques have been used to treat NPC in the past, namely 2-dimensional radiotherapy (2DRT), conventional 3-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT). Among the various types of radiotherapy, IMRT is becoming more widely used for treating head and neck cancer over conventional 2DRT and 3DCRT in recent years (Bucci, Bevan, & Roach, 2005), because IMRT has recognized better target coverage and sparing of normal organs. IMRT has also been used since a clinical investigation in the 2000s in Hong Kong and promising results for loco-regional control was presented (Kam et al., 2004). Advantage in swallowing-related outcome has been reported. IMRT can, for example, induce less severe xerostomia and reduced the penetration or aspiration (Kam, Chau, Suen, Choi, & Teo, 2003; Mortensen, Jensen, Aksglaede, Behrens, & Grau, 2013; Vergeer et al., 2009; Xia, Fu, Wong, Akazawa, & Verhey, 2000). Hence, it is likely that the trend

found in this study can be affected by the improvement in radiotherapy technique. In light of this, further study on factors associating with swallowing outcome should involve prospective evaluation of swallowing outcome with collection of treatment-related factors. Upon identification of factors associated with long-term dysphagia, NPC survivors prone to long-term dysphagia might be easier to identify and hence early intervention for at-risk groups can be provided.

Despite the need to further investigate the factors associated with long-term swallowing outcomes such that early identification is possible, there is a also strong need to investigate ways through which the swallowing dysfunctions could be minimized. Reduction of doses to certain structures seems to be a promising direction (Eisbruch et al., 2004). In view of the capability of IMRT in sparing more normal organs, studies are steering to identify ways to optimize radiotherapy for better swallowing outcomes. For example, emerging evidence suggests that dose to certain swallowing-related structures are significantly correlated with swallowing difficulties (Feng et al., 2007; Levendag et al., 2007) Hence, further research direction should also focus on whether modification to treatment parameters such as dosage can reduce long-term swallowing problems in nasopharyngeal cancer survivors with multidimensional evaluation of swallowing functions. Also, after specific factors which are associated with long-term swallowing outcome are identified, alteration to the specific parameters, if feasible, might also help optimize swallowing outcomes. Yet, this should also be investigated further in prospective studies.



### Conclusion

This study showed that long-term swallowing problems were prevalent in nasopharyngeal cancer survivors. Oromotor deficits, penetration or aspiration and pharyngeal retention were common long-term swallowing problems. The swallowing problems also manifested in limiting their day-to-day activities and participation in life events, though large variation in functioning was noted. Further analysis indicated that radiotherapy concurrent with chemotherapy was associated with lower degree of penetration and less pharyngeal retention than radiotherapy alone. Correlation analysis showed that the degree of penetration, pharyngeal retention increased with time since completion of radiotherapy and functioning in the activity and participation domains decreased with time since completion of radiotherapy. The results indicated that continuous monitoring of swallowing functions is necessary for nasopharyngeal cancer survivors. Further research is needed to identify other factors which are associated with swallowing outcomes such that early identification of at-risk survivors is feasible. Also, further research on ways to minimize long-term swallowing problems should be conducted.

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